10/511748
DT01 Rec'd PCT/PTC 19 OCT 2004

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (original) A cell population prepared from blood mononuclear cells, said mononuclear cells being peripheral blood mononuclear cells (PBMC) or CD14+ monocytes, said population containing from about 5 % to about 50 % of activated mononuclear antigen presenting cells (APCs) having the following characteristics:

- they express surface markers CD2, CD83 and CD14, MHC class I and MHC class II molecules
- they secrete TNF-α
- they are able to stimulate allogenic T lymphocytes, as shown by mixed lymphocyte reaction (MLR) measurements.

2. (currently amended) The **[[A]]** cell population prepared according to claim 1, characterized in that activated mononuclear APCs are able to stimulate autologous T lymphocytes proliferation in the presence of a specific antigen.

3. (original) Activated mononuclear APCs prepared from blood mononuclear cells and having the following characteristics:

- they express surface markers CD2, CD83 and CD14, MHC class I and MHC class II molecules
- they secrete more than 50 pg/ml of TNF-α
- they are able to stimulate allogenic T lymphocytes, as shown by MLR measurements.

4. (original) Activated mononuclear APCs according to claim 3, characterized in that they express the following surface

markers: CD2, CD14, CD83, CD54, CD58, CD86, MHC class I and MHC class II molecules.

5. (currently amended) Activated mononuclear APCs according to claim 3 [[or 4]], characterized in that they are able to stimulate autologous T lymphocytes proliferation in the presence of a specific antigen.

6. (currently amended) Activated mononuclear APCs according to claim 3 ~~any one of claims 3 to 5~~, characterized in that they possess phagocytic properties, as shown by dextran-uptake capability.

7. (currently amended) Activated mononuclear APCs according to claim 3 ~~any one of claims 3 to 6~~, characterized in that they do not secrete detectable levels of IL-10 and secrete less than 100 pg/ml of IL-12.

8. (currently amended) Activated mononuclear APCs according to claim 3 ~~any one of claims 3 to 7~~, said activated mononuclear APCs having been loaded with antigenic peptides or proteins, with a cellular extract containing at least one antigen or with nucleic acid molecules.

9. (currently amended) A method for preparing mononuclear Antigen Presenting Cells comprising treating said cells with ~~Use of~~ ligands having receptors on the surface of blood monocytes, of cytokines having receptors on the surface of blood monocytes, of inducers of interferon synthesis by blood mononuclear cells, or of a physical stress, or a combination thereof, as means allowing the preparation from blood mononuclear cells in an appropriate medium, for about one to about five hours and preferably for less than about four hours, of a cell population according to claim 1 ~~or 2~~

or of activated mononuclear APCs ~~according to any one of claims 3 to 8, said means being applied to the mononuclear cells from the initial stage of the preparation~~.

10. (currently amended) The method, ~~A use~~ according to claim 9, wherein said ligand is chosen among the group consisting of: cell growth factors, complement polypeptides, muramyl dipeptide analogues, natural and synthetic detoxified endotoxin derivatives, histamine, vitamin D3, arachidonic acid metabolites, aminosulfonic acid derivatives, bacillus Calmette-Guérin and bacterial membrane extracts.

11. (currently amended) The method ~~A use~~ according to claim 9, wherein said cytokine is type I IFN and is selected from the group consisting of: any natural IFNα, any recombinant species of IFNα, natural or recombinant IFNβ and any synthetic type I IFN.

12. (currently amended) The method ~~A use~~ according to claim 11, wherein said type I IFN concentration in the medium is in a range of about 100 to about 100.000 IU/ml~~, and preferably in a range of about 1.000 to about 10.000 IU/ml~~.

13. (currently amended) The method ~~A use~~ according to claim 9, wherein said cytokine is chosen among the group consisting of: IFN gamma, IL-12, IL-13, IL-18, GM-CSF, TNFα and TGFβ.

14. (currently amended) The method ~~A use of a cytokine~~ according to claim 9 ~~or 13~~, wherein said cytokine concentration in the medium is in a range of about 0.01 ~~0,01~~ to about 10 µg/ml ~~and preferably in a range of about 0,1 to about 1 µg /ml~~.

15. (currently amended) The method ~~A use~~ according to claim 9, wherein said medium contains type-I interferon, at a

concentration of about 10.000 IU/ml, and GM-CSF, at a concentration of about 500 IU/ml.

16. (currently amended) The method ~~A use~~ according to claim 9, wherein said physical stress consists of one of the following events:

- the separation of blood mononuclear cells from the plasma contained in the blood initially containing the mononuclear cells,
- the exposure of the blood mononuclear cells to an osmotic change,
- the exposure of the blood mononuclear cells to an electrical field or
- the exposure of the blood mononuclear cells to a temperature variation of +/- 3 to 8°C from 37°C.

17. (currently amended) A process for preparing, from blood mononuclear cells, a cell population according to claim 1 ~~or 2~~, or activated mononuclear APCs ~~according to any one of claims 3 to 8~~, comprising a step of contacting said mononuclear cells with an appropriate medium, for about one to about five hours and preferably for less than about four hours.

18. (currently amended) The **[[A]]** process according to claim 17, characterized in that said medium contains, from the initial stage of the preparation, a component selected from the group consisting of: ligands having receptors on the surface of monocytes, cytokines having receptors on the surface of monocytes and inducers of interferon synthesis by blood mononuclear cells or a combination thereof .

19. (currently amended) The **[[A]]** process according to claim 18, wherein said ligand is chosen among the group consisting of: cell growth factors, complement, muramyl dipeptide analogues,

natural and synthetic endotoxin derivatives, histamine, vitamin D3, arachidonic acid metabolites, aminosulfonic acid derivatives, bacillus Calmette-Guérin and [[or]] bacterial membrane extracts.

20. (currently amended) The [[A]] process according to claim 19, wherein said cytokine is type I IFN and is selected from the group consisting of: any natural IFNα, any recombinant species of IFNα, natural or recombinant IFNβ and any synthetic type I IFN.

21. (currently amended) The [[A]] process according to claim 20, wherein said concentration of type I IFN in the medium is in a range of about 100 to about 100.000 IU/ml~~, and preferably in a range of about 1.000 to about 10.000 IU/ml~~.

22. (currently amended) The [[A]] process according to claim 18, wherein said cytokine is chosen among the group consisting of: IFN gamma, IL-12, IL-13, IL-18, GM-CSF, TNFα and TGFβ.

23. (currently amended) The [[A]] process according to claim 22, wherein said concentration of cytokine in the medium is in a range of about 0,01 to about 10 μg/ml and preferably in a range of about 0,1 to about 1 μg/ml.

24. (currently amended) The [[A]] process according to claim 23, wherein said medium contains type-I interferon, at a concentration of about 10.000 IU/ml, and GM-CSF, at a concentration of about 500 IU/ml.

25. (currently amended) The [[A]] process for preparing, from blood mononuclear cells, a cell population according to claim 1 ~~or 2~~, or activated mononuclear APCs ~~according to any one of claims 3 to 8~~, comprising a step of exposing said blood mononuclear cells to a physical stress, which can be: the separation of blood mononuclear cells from the plasma contained in

the blood initially containg the mononuclear cells, the exposure of the cells to an osmotic change, to an electrical field or to a temperature variation of +/- 3 to 8°C from 37°C.

26. (currently amended) The **[[A]]** process according to claim 18 ~~any one of claims 18 to 25~~, wherein said medium also contains antigenic peptides or proteins, a cellular extract containing at least one antigen or nucleic acid molecules.

27. (currently amended) The **[[A]]** process according to claim 18 ~~any one of claims 18 to 25~~, wherein said process comprises:

- a first step of contacting mononuclear cells with an appropriate medium for about one to about five hours and preferably for less than about four hours, for the preparation of activated mononuclear APCs
- a second step of contacting said activated mononuclear APCs with a maturation agent.

28. (currently amended) Activated mononuclear APCs such as obtained by a process according to claim 17 ~~any one of claims 17 to 25~~.

29. (currently amended) A cell population according to claim 1 ~~or 2~~, or activated mononuclear APCs ~~according to any one of claims 3 to 8 and 28~~, wherein activated mononuclear APCs are kept under a frozen form, in an appropriate cryo-preservative solution.

30. (cancelled)

31. (cancelled)

32. (currently amended) A kit for preparing, from blood mononuclear cells, a cell population according to claim 1 ~~any one of claims 1, 2 and 29~~ or activated mononuclear APCs ~~according to~~

~~any one of claims 3 to 8 and 28~~, in a close system allowing the exclusion of any conventional ex-vivo culture step and comprising at least:

-single use elements necessary for the culture and the washings of the cells, including bag(s), culture medium, buffers and connecting tube(s), including connecting tube(s) to an apheresis machine.

-possibly a composition comprising type I IFN and compatible additives,

-possibly a composition comprising a cytokine and compatible additives,

-possibly a composition comprising a ligand having receptors on the surface of blood monocytes and compatible additives,

-possibly a composition comprising a cell growth factor and compatible additives,

-possibly a composition comprising at least one antigen, or nucleic acids coding for at least one antigen, to which an immune response is of interest .

33. (currently amended) A pharmaceutical composition or a vaccine comprising, as active principle, activated mononuclear APCs according to claim 3 ~~any one of claims 3 to 8, 28 and 29~~, together with a pharmaceutically acceptable carrier vehicle or an auxiliary agent, in an amount of about 10^5 to about 10^{10}~~, and preferably about 10^7 to about 10^8~~ of said cells per dose administered.

34. (currently amended) A pharmaceutical composition or a vaccine containing, as an adjuvant of an active principle, activated mononuclear APCs according to claim 3 ~~any one of claims 3 to 8, 28 and 29~~, in an amount of about 10^5 to about 10^{10}~~, and preferably about 10^7 to about 10^8~~ of said cells per dose administered.

35. (currently amended) A method for treating an infectious or neoplastic disease in a patient, comprising administering an effective amount of ~~Use of~~ a cell population according to claim 1 to said patient in need thereof ~~any one of claims 1, 2 and 29, or activated mononuclear APCs according to any one of claims 3 to 8, 28 and 29, for the manufacture of a medicament for treating an infectious or neoplastic disease~~.

36. (new) A method for treating an infectious or neoplastic disease in a patient, comprising administering an effective amount of activated mononuclear APCs according to claim 3 to said patient in need thereof.